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SCIENCE AND TECHNOLOGY

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JAPAN REPORT

SCIENCE AND TECHNOLOGY

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R&D ACTIVITIES IN FY 1984 SUMMARIZED

Tokyo SEIMEI KOGAKU in Japanese Mar 85 pp 19-40

[Excerpts] Domestic Issues

Industry

January

Takara Shuzo Co.

Starts to sell the electrophoresis system, "TAKARA-VEI" for genetic engineering.

Hayashibara Biochemical Laboratories

Cooperation with Denmark Novo Industry. It supplies the production method of enzyme with radioactivity.

Takeda Chemical Industries

Decides to start large-scale production of gamma interferon by April.

Sumitomo Chemical Co.

Announced to develop new fields including new seeds and seedlings produced by tissue culture technology.

Universities and research institutes

January

The Institute of Physical and Chemical Research

Will start to distribute microbial strains. In FY 1984 they will provide 610 strains of bacteria, fungi, and yeast.

The Saikai-ku Institute of Fishery

Succeeded in dissolving cell wall of seaweed for cell fusion.

National Hygenic Laboratory

Developed monoclonal antibodies against human red blood cells by cell fusion of human tumor cell with spleen cells of mouse which was immunized with human red blood cells.

Government ministries and organizations

January

Foundation for Cancer Research Promotion

Decided to accept gene bank project as one of 10 projects of anti-cancer research.

The Ministry of Agriculture, Forestry and Fisheries [MAFF]

Pursues the improvement in food production utilizing bioreactors for the food industry. They organize private companies to promote development of bioreactors in 5-year plan starting 1984.

Industry	Universities and research institutes	Government ministries and organizations
Shimazu Seisakusho & Wakunaga Pharmaceutical Announced to develop and market automatic DNA synthesizer.	Food Technology Laboratory of Aichi Prefecture Decided to develop the rapid fermentation method for the production of vinegar using bioreactor.	
Suntory Cooperation with Rockefeller University, New York, in new area of brain and nerve biotechnology, and nerve physiology.	The Group of Professor Kobayashi of Nagoya University Succeeded in developing yeast with alcohol fermenting ability using cell fusion technology.	
Software Development Co. Starts to sell automatic data input system for the determination of nucleic acid base sequences.	The Institute of Physical and Chemical Research Started to build laboratory for genetic engineering.	
C. Itoh & Co., Ltd. Engages in plant seed business and tries to establish trading opportunity in China.		
The Green Cross Corp. Discontinued the contract with U.S. CRI concerning the interferon production. One reason is that the company has not obtained research results from CRI and the second reason is that The Green Cross Corp. has already established the genetic engineering technology to produce interferon by itself.		

Industry	Universities and research institutes	Government ministries and organizations
Nissho-Iwai Co., Ltd. & UGEN Established cooperation and began marketing in biotechnology. Mitsui Engineering & Shipbuilding Co., Ltd. Established the development section to engage in biotechnology plant building.		
February	February	February
Nissho-Iwai Co., Ltd. Starts the seed business by investing capital in SGI. Japan Roche & Takeda Chemical Industries Developed the procedure for the gamma interferon production by genetic-engineering; its clinical test will start in April. Mitsui Pharmaceutical Co. Ltd. Announced the cooperation with Canadian (Furapie) to produce pharmaceuticals by biotechnology. Hayashibara Biochemical Laboratories Patent of the production of monoclonal antibody will be established in the United States by the end of this year. This	Chemical and Sero-therapy Institute Announced the establishment of procedure to produce hepatitis virus B vaccine. Noticing that the surface antigen of HBV (HBs Ag) has high immunity including activity, they cloned HBs Ag gene from HBV core and inserted it into yeast to produce HBV vaccine. Professor Anraku of the University of Tokyo Succeeded for the first time in the world in purifying membrane proteins. Cytochrome b which is an enzyme for bacterial respiratory reaction in E. coli membrane and adenosine-triphosphate decomposition enzyme (ATPase) to produce energy in yeast vacuol membrane were purified.	Science and Technology Agency [STA] Announced fiscal 1984 governmental budget of Y4.5 billion for the 10 year project of anticancer research. Patent Office Discusses biotechnology patent in terms of its operation and guidelines. Ministry of International Trade and Industry [MITI] Started to engage in education of biotechnology engineers for private sector. Science and Technology Council Determined the guideline for recombinant DNA should be introduced into neither human body nor primate fertilized ova. The animal integrated with

Industry

patent was published in May 1983; title: procedure to propagate anti-human protein antibody.

Ajinomoto

Declared to proceed with animal test of IL-2 produced by genetic engineering.

Toyobo

Manufactured host vector system for Bacillus subtilis, streptomyces, and yeast.

The Green Cross Corp.

Starts clinical test of gamma-interferon produced by cell culture procedure using leucocyte cell line.

Sumitomo Chemical Co.

Applied for permission for natural alpha-interferon production.

Universities and research institutes

National Institute of Agroenvironmental Sciences

Succeeded in the isolation of cytoplasmic DNA of vegetable withering fungi which has information to make cells resistant to pathogenic bacteria.

National Chemical Laboratory for Industry

Established new technique for the chemical synthesis of DNA. This is the procedure using polystyrene powder carrying nucleotides for the synthesis of DNA in a glass reaction vessel. It requires 3 days to synthesize DNA for which the existing procedure takes 3 months.

Professor Murakami of Tsukuba University

Completed the three dimensional model of human renin enzyme gene.

Government ministries and organizations

the recombinant DNA should be isolated and not be duplicated. The bodies and their waste must be treated carefully. Researchers should report every half year. The recombinant DNA experiment in plants should be done under the condition of isolation and the protection against the scattering of pollens and seeds.

Japanese Organization of Seed and Seedlings

Determined the five companies which will be engaged in the 5-year project of plant breeding by tissue culture. The project will start in 1983. They are Tohoku Seed and Seedlings (Tochigi), Hokuetsu Noji (Niigata), Simizu Seed and Seedlings (Nagano), Fujii Nosan (Oosaka), and Hachiye Nogei (Nagasaki).

MAFF

Starts research on cultivation of experimental seeds by commission to universities and firms.

STA and New Technology Development Organization

Fixed the three major projects of cancer research. These are: (1) Development of DNA

Industry	Universities and research institutes	Government ministries and organizations
		base sequence analyzer. (2) Development of membrane for electrophoresis for the sequencing of DNA base. (3) Development of immunotherapy using denatured DNA.
		MAFF Announced that they are not in favor of issuing patent for the new variety of plant. The first plant patent applied by Nihon Shinyaku for their new variety of mugwort which is used to get rid of mawworms. They are afraid that the patent might disturb farming management.
March	March	March
Sumitomo Shoji Kaishi Co. and Kyowa Hakko Kogyo and NPI, United States Agreed to cooperate in development of seed using biotechnology. The three companies will establish seed development company in Singapore in the near future.	The Institute of Physical and Chemical Research Started genetic engineering experiment using lacto-bacillus in P4 containment laboratory.	Science and Technology Council Completed the developmental plan of life science research by clarifying main targets and procedures for promotion.
Shiseido Declared to manufacture so-called biocosmetics in these 2 years.	National Institute of Animal Health Succeeded in development of monoclonal antibody against swine chorella using swine lymphocyte cell fusion.	MITI Announced that they will establish international organization to promote international cooperation which is based on the summit talk.
Toyo Jozo Co. Declared to cooperate with New York State University to study oncogenes.	National Institute of Radiological Sciences Discovered the "repair gene" which repairs DNA damaged by ultraviolet ray irradiation. Masaaki Hori, chief	STA Cooperates with ASEAN countries to search for biological resources.

Industry	Universities and research institutes	Government ministries and organizations
Maruzen Biochemical Co. Declared to cooperate with Software Development Co. to develop nucleic acid base sequence input apparatus. Kyowa Seed and Seedlings Co. and Plant Technology Institute Declared to cooperate in the production of "biovegetables."	researcher of genetics section has discovered and named it "ERCM2." National Institute of Genetics Developed the very rapid DNA sequencing technique, shotgun DNA sequencing technique. They sonic analyzed the NDA to shorten the length of it and subcloned the fragmented DNA into M13 bacteriophage and analyzed DNA base sequences by the aid of computer to obtain the complete structure of the DNA.	The Organization for the Exchange of Information on Agriculture, Forestry, and Fisheries Decided to develop research on cell fusion technology. STA Succeeded in analyses of genetic aberration caused by irradiation in monkeys. MAFF Established biotechnology section to promote the interdisciplinary development of biotechnology.
April Kaneko Seed and Seedlings Co. and Nakajina Tenko-en and Sumitomo Shoji Kaisha and Kyowa Hakko Kogyo Cooperate in the development of "bioseeds and seedlings." C. Itoh & Co. Engaged in seed business through cooperation with (DENFERT). Kyowa Hakko Kogyo Succeeded in production of sugar by converting biomass in a large scale reaction tank.	April Cancer Institute Succeeded in mass production of protein of adult T lymphocyte leukemia virus. Under the cooperation with Kyowa Hakko Kogyo, they introduced a part of the ATL virus gene into E. coli to produce viral protein as they did for the production of interferon. More than 10 percent of the protein produced in E. coli is the viral protein, thus it is possible to mass produce the viral protein. Group of Professor Fukui of Hiroshima University Succeeded in propagating new variety of yeast by genetic engineering.	April Ministry of Health and Welfare Determined the standard for the approval of pharmaceuticals made by genetic engineering. Even if the pharmaceuticals made conventionally were approved already, if it is produced by the recombinant DNA technology, the company should prepare examination data of more than 20 categories for its safety and validity as if it were a newly developed drug. STA Started investigation on chromosome manipulation technology.

Industry	Universities and research institutes	Government ministries and organizations
Mitsubishi Chemical Industries and Nagoya University Succeeded in secreting protein produced in genetically engineered cell. The procedure is: 1) Cleavage of the gene for the signal peptide of 22 amino acids out of Omp-F gene of E. coli. 2) Connection of the signal peptide gene with the gene of desired protein like beta-endorphin, and 3) Introduction of the connected gene into E. coli and expression of the gene in the bacteria. Mitsui Petroleum Chemistry Co. Manufactured biodyes by utilizing gromwell.	National Institute of Agrobiological Resources Will perform genetic engineering experiment in tobacco plant to produce protein. The experimental plan applied by them was approved by the Science and Technology Council. They will integrate kidney beam protein (phaseolin) DNA into cultured tobacco and petunia cells and propagate them to plant.	MAFF Started to study the culture of shoot apex. MAFF Started to enlarge the seed data bank. Science and Technology Council Suggested to develop genetic engineering in higher plants and animals. MAFF Established the research organization composed of 11 private firms for the development of bioagrochemicals.
May	May	May
The Green Cross Corp. Succeeded in analyzing urokinase gene. They extracted mRNA from cultured human kidney cells and cDNA was cloned, and determined the nucleotide sequences of the cDNA. Nippon Reizo K.K. Declared to build new company for the plant breeding research.	National Institute of Chemical Technology Succeeded in development of mass production technology for gamma linoleic acid. Ooyama, research associate of Kyoto University Developed the new technique to utilize choroplast DNA as vector in plant recombinant DNA technology.	STA Succeeded in mass production of electrophoresis membrane and development of computer software for the determination of the secondary structure of DNA the bass sequence of which is known. STA Succeeded in the production of hepatitis B virus vaccine by genetic engineering. This is a result of

Industry	Universities and research institutes	Government ministries and organizations
Kyowa Hakko Kogyo Succeeded in improvement in cellulase producing bacteria. Sumitomo Chemical Industries Developed a procedure for root culture. Shionogi and Co. Applied for permission for insulin production by genetic engineering. They will use E. coli in which human insulin gene was introduced by Eli-Lilly of the United States to produce insulin.	Tochigi Agricultural Research Institute Succeeded in mass production of strawberry seedlings utilizing growth point culture. Instructor Takahisa of Chiba Institute of Technology Succeeded in the chemical synthesis of DNA of dinorphine which has the most potent pain-killing activity.	Akira Ooya's experiment, the chief researcher of rickettsia section of National Institute of Health. He is also a leader of the research project called "vaccine production by utilizing genetic engineering" which is promoted by the Agency. They succeeded in the production of hepatitis B viral antigen in yeast manipulated by genetic engineering. National Institute of Agrobiological Resources Announced to prepare the data base of sorghum and barley seeds.
June Meiji Seika Started clinical test of interferon. Takeda Chemical Industries Started clinical test of IL-2 produced by genetic engineering. Dai-Nippon Pharmaceutical Co. Started to sell blood clot dissolving agent which is the first product of biotechnology Dai-Nippon Pharmaceutical Co., Dynabot, Kyorin Pharmaceutical Co., and Mitsubishi	June Keio University, School of Medicine Succeeded in discovering cancer gene of human hepatoma. Tatsuya Nakamura and Toshio Morimi of digestive organ and gastroenterology section have isolated the cancer gene of human hepatoma from a patient who died of hepatoma after HBV infection. They transformed NIH 3T3 mouse cell line with DNA prepared from hepatoma tissue of the patient, and detected	June MAFF Announced to distribute crop plant genetic resources to private sectors. MAFF Decided to develop breeding technology for fisheries utilizing chromosomal manipulation.

Industry	Universities and research institutes	Government ministries and organizations

Petrochemical Pharmaceutical Co. have cooperated in manufacture of urokinase which is produced by tissue culture. The urokinase was produced by Abbott Laboratories of the United States and imported for injection use.

Hayashibara Biochemical Laboratories

Started to build the largest cell culture center in the world.

Mitsubishi Corp.

Invested capital in Bio-Beck Technology in the United States.

Fujisawa Pharmaceutical

Succeeded in mass production of growth hormone "somatomesin C" by genetic engineering.

The Green Cross Corp.

Succeeded in gamma-interferon production by genetic engineering.

Toyo Engineering

Established new bio-engineering company under joint management with BWA of the United States.

Sumitomo Chemical Industries

Started to build commercial plant to produce interferon.

human oncogene "K-ras" in the transformed NIH 3T3 cell line. The "K-ras" oncogene has been detected in several human cancers including colon cancer. They concluded that the "K-ras" oncogene in human hepatoma transformed NIH 3T3 cell line.

Professor Beppu of Tokyo University

Succeeded in the isolation and the structural analysis of regulatory gene in streptomyces which produces antibiotics. This regulatory gene has an inducing activity of repressed antibiotics synthesis genes. This is useful for the new antibiotics development and mass production of antiobiotics.

Research Institute for Microbial Diseases, Osaka University

Succeeded in the preparation of "hybrid bacteria" by genetic engineering. This hybrid bacteria is used for the determination of mutation inducing rate of food and chemicals, and developed by Hideo Shinagawa, a research associate of the Institute. Seiich Nakamura, the chief researcher of workers hygiene division of Osaka Institute of Health has confirmed the function of the bacteria.

Industry	Universities and research institutes	Government ministries and organizations
July	July	July
Suntory Succeeded in production of "gamma-hamp," the urination and reduction of blood pressure hormone, by genetic engineering. They have been cooperated with Miyazaki Medical College to determine 126 amino-acid sequences of the hormone. The base sequence of the hormone gene was then determined from the amino acid sequence by the principle that one amino acid is determined from the three base sequences of the DNA. They produced the hormone in E. coli into which the hormone DNA was introduced by genetic engineering.	**Group of Professor Honjo of Kyoto University** Clarified the structure of T-cell receptor gene.	**Ministry of Health and Welfare** Determined six projects for its 10 year anticancer research.
Shionogo and Company Announced a cooperation with Merck of the United States, to develop and produce HBV vaccine by genetic engineering.		**MAFF** Announced to start three research projects for the cultivation of technical seeds of biotechnology. These three projects are: 1) marine microorganisms, 2) artificial enzymes, and 3) gene expression.
Takeda Chemical Industries Started the clinical trial of IL-2, immunopotentiator and antitumor agent.		**MAFF** Decided to distribute five parental strains of new varieties including tomato.
Toyo Menka Kaisha, Ltd. Started to engage in biotechnology business by cooperation with IRI of Great Britain.		**STA** Decided to apply for the next year governmental budget of Y100 million for the establishment of gene bank.
		STA Decided to build a facility for the collection of wild plants.

Industry	Universities and research institutes	Government ministries and organizations
Hitachi Chemical Co. Establishes research institute for biotechnology in the University of California, Irvine, to promote research and development of biotechnology.		
Nippon Mushroom Research Institute Succeeded in cell fusion of two kinds of mushroom cells.		
Hitachi Software Engineering Co. Started to sell the DNA base sequence analyzing system.		
Morinaga Confectionary Co. Succeeded in production of human monoclonal antibody. They succeeded in production of human monoclonal antibody which reacts specially with established lung cancer cell lines by the basic biotechnology of cell fusion among human cells, through the cooperation with Professor Hiroki Murakami of the Kyushu University.		
Mitsubishi Corp. Started to sell exclusively new seeds through capital investment in Sun Gene of the United States.		

Industry

August

Mitsui Group

Reached an agreement to cooperate in manufacture of plant organ culture.

Research Organization of Agricultural Biotechnology Development

Started to study biological insecticides by assigning the procedures among organized companies.

The Green Cross Corp.

Succeeded in production of prourokinase, the precursor of urokinase, by genetic engineering. This precursor has a molecular weight of 54,000 and composed of a chain polypeptide which has an affinity with fibrin and 20,000 in molecular weight and B chain polypeptide which has blood clot dissolving activity and 32,000 in molecular weight. These polypeptides are combined to form single strand polypeptide in its primary structure.

September

NEC Corp.

Succeeded in production of one-chip IC biosensor integrated with oxygen membrane. The IC chip sensor developed has a sapphire base on which two silicon FET's of

Universities and research institutes

August

National Institute of Animal Industry

Succeeded in the propagation of twin goat by embryo cleavage.

Mayeda, a research associate of Tottori University

Succeeded in mass production of interferon in silk worm by genetic engineering.

National Institute of Agrobiological Resources

Succeeded in the analysis of viral RNA which causes a disease in vegetables by genetic engineering. They have discovered the small difference of RNA sequence of a virulent virus and the attenuated virus which is used as a vaccine. They determined all the RNA sequence of tobacco mosaic virus of tomato (a virulent virus) and the attenuated virus.

September

Fermentation Research Institute

Will start to construct the facility to accept microorganisms for patent application next year.

Government ministries and organizations

August

The Ministry of Agriculture, Forestry and Fisheries

Announced the start of interdisciplinary cooperation in seed research.

MAFF

Established the interdisciplinary council to develop biotechnology effectively.

STA

Announced to start promoting council for the assurance of genetic resources.

MITI

Accepted the biochip research project for "the fundamental technology research development program for the industry of next generation."

STA

Announced to establish gene bank at Ibaraki.

September

MAFF

Decided to start breeding for fisheries.

Industry	Universities and research institutes	Government ministries and organizations

npna pole structure were grown epitaxially. Silica dioxide and silica boronite membranes were put on it to form transistor structure, and finally the uppermost surface was coated with activated oxygen membrane.

Kanegafuchi Chemical Industry

Succeeded in cell culture of animal cells to produce human gamma interferon. They established technology to grow hamster cells into which the human interferon gene was integrated.

Shiseido

Succeeded in mass production of hyaluronic acid, a cosmetics raw material, by biotechnology.

Toyobo

Started to produce tissue type plasminogen activator (TPA) by genetic engineering through cooperation with Genetics Co. of the United States.

Suntory

Succeeded in production of interleukin 2 secreted from yeast.

Nippon University and Sata Medical College

Succeeded in the integration and expression of human genes in mice. Yamamura, an instructor of Nippon University, School of Medicine and Professor Watanabe of Saga Medical College have injected human gene into mouse fertilized ova and transplanted them to oviduct of the pseudopregnant mouse resulting in the birth of offspring which have human gene integrated in cells.

Cancer Institute, other institutes

Discovered the viral product of blood cancer virus.

New Technology Development Corporation

Started the research project of "super microorganism." One of the projects of the creative science and technology promoting systems of the STA is Professor Horikoshi's project of research on microorganisms which grow under extreme environmental conditions. They will start to collect strong microbials which grow at high temperature, pressure, or aklaline condition. Genetic engineering techniques will be adopted to transfer those strong activities into bacteria which

MAFF

Decided to start breeding for fisheries.

Industry	Universities and research institutes	Government ministries and organizations

produce sugar or amino acids. These bacteria will be applied to chemical reactions which now require high temperature and/or pressure.

Industry

October

Chugai Boeki Co.

Announced intention to engage in biotechnology field by capital investment in a company in the United States.

Sankyo Co.

Enlarged the cooperation with Celltech of Great Britain to develop antitumor agents.

University of Tokyo, Dainippon Pharmaceutical Co. and Asahi Chemical Industry

Started tumor necrosis factor (TNF) clinical trial. This is the first time of the clinical test of TNF which was developed by Dr Haranaka of the Institute of Medical Sciences.

Kanebo Ltd.

Succeeded in mass production of aromatic plant by plant tissue culture. The tissue culture procedure newly developed is called an uncertain bud (stem and leaf) differentiation culture. The weight of

Universities and research institutes

October

National Cancer Center

Announced that an oncogene has an indispensable role in keeping cells alive. Takeshi Hayashi and Suzuko Makino have discovered that the oncogene (myc) was activated after partial hepatectomy in a mouse.

Shimizu, a research associate of Kyushu University

Discovered a new stomach cancer gene for the first time. They transfected normal cells with DNA isolated from cancer cells of stomach cancer patient resulting in the transformation of the normal cells into tumor cells. Afterwards, they repeated the experiment successfully using DNA isolated from the transformed cells. They identified the tumor gene, which has 50,000 base pairs in length and referred to X-2, in DNA isolated from the tumor cells. Other than X-2 gene, they identified the X-1 gene which resembles the well-known (ras)

Government ministries and organizations

October

STA

Established the promoting council for the assurance of genetic resources.

MITI

Decided to establish the guideline for the biotechnology application to the industrial production.

Industry	Universities and research institutes	Government ministries and organizations
aromatic plant tissue increased from 10 grams to 400 grams in 3 weeks. Mitsubishi Chemical Industries Succeeded in the regeneration of cabbage starting from one independent cell.	oncogene. They purified the X-2 gene with more than 70 percent purity. Though the X-1 gene could not be purified so far, it is possible that X-1 gene is also a tumor gene because it induces tumor in nude mice. National Institute of Agrobiological Resources and Nagoya University Succeeded in the protoplast culture of rice cells. Professor Shimizu of National Aerospace Laboratory Succeeded in the clarification of the mechanism of discrimination of amino acids by transfer RNA. He reacted amino acids and genetic codons in water and found that the codons and amino acids bind specifically. National Chemical Laboratory for Industry Considers to utilize immobilized enzyme system for biosynthesis of prostagladin. Professor Arai and his colleagues of Tsukuba University Succeeded in the seed culture of mice to produce ovule for the first time in the world.	

Industry	Universities and research institutes	Government ministries and organizations
November	November	
Wakunaga Pharmaceutical Stopped the development of secretin because of the difficulty in the stabilization of the structure.	The Institute of Physical and Chemical Research and Pasteur Institute Started to cooperate in biotechnology research between Japan and France.	
Toray Succeeded in production of natural beta interferon by animal cell culture. Ajinomoto and Cancer Institute Announced to offer the IL-2 production patent to Roche of the United States.	The Kitasato Institute Succeeded in new antibiotics production by genetic engineering. Ohmura of the Institute in cooperation with Professor Hopwood of John Innes Research Institute of Great Britain have improved a strain of actinomyces to produce completely new antibiotics by genetic engineering.	
Kyowa Hakko Kogyo Developed the procedure to produce phenylalanine, the material to produce synthetic sweetener, by genetic engineering. They introduced genes for enzymes which participates in the production of phenylalanine into bacteria producing phenylalanine. They produced phenylalanine through fermentation using the transformed bacteria.	Professor Numa of Kyogo University Clarified the structure of information transducing material which transfer information from brain to body organs. The gene structure of the protein of sodium channel which is a fundamental signal transducing apparatus located in nerve cells was determined for the first time.	
Sumitomo Chemical Co. and others Succeeded in production of detoxicating enzyme in E. Coli and yeast. This is the enzyme produced in animal liver and called		

Industry	Universities and research institutes	Government ministries and organizations
"cytochrome P-450." This material was produced in E. coli and yeast which were manipulated by genetic engineering to produce the cytochrome P-450.		
December	December	December
Takeda Chemical Industries Succeeded in production of interferon in bacillus subtilis. Kyowa Hakko Kogyo and Kitasato University Succeeded in mass production of white salmon growth hormone using genetic engineering. Ajinomoto Announced that IL-2, immune potentiator protein, has antitumor activity. Mitsubishi Chemical Industries Succeeded in mass production of (apo) protein using biotechnology. (Apo) protein reduces hardening of blood vessel walls which causes high blood pressure and some heart diseases. They established the technology to produce E type apo-protein among several kinds of apoproteins.	Associate Professor Hotta of Tokyo University Succeeded in the gene therapy in drosophila with abnormal wings. Osaka University Succeeded in the expression of human gene in a mouse. Instructor Kenichi Yamamura of the School of Medicine and his colleagues integrated human histocompatibility gene in mice. They mass produced the human DNA in genetically engineered E. coli, introduced the DNA into 500 fertilized mouse eggs and returned them into the mice. Four out of thirty offspring have human histocompatibility genes integrated into chromosomes and utilize the information of the DNA for their own immune reaction. A group of Tokyo Metropolitan Institute of Aging Succeeded in the expression of human tumor gene in mice. Shinichi Aizawa, a head researcher, injected human ras oncogene isolated	Patent Office Established the guideline for genetic engineering patents. The new guideline permits some exceptions for the duty to deposit the microorganism and cells newly developed to the public facilities; that is, the patent could be applied only with documents. The Environment Agency Announced the result of investigation on the dependence of DNA microorganisms existence on protozoa injection. Federation of Economic Organizations Discussed biotechnology patents on three points: 1) the coverage of patents, 2) classification of patents, and 3) relationship of patents to international movements.

Industry	Universities and research institutes	Government ministries and organizations
The Green Cross Corp. Applied for the permission of new type alpha-interferon production.	from human bladder cancer into 12-hour old mouse fertilized ova and transplanted them into mouse oviducts. Sixty-four offspring were born after 3 weeks and 5 of them have integrate human oncogene. Professor Murakami of Tsukuba University Started mass production at renin gene. Microbiology Laboratory of Tokyo University Developed new vector for yeast, Saccharomyces cerevisiae. This vector plasmid is very stable in yeast cells, that is, 70-90 percent of cells still harbor the plasmid after 10 generations of growth. It is easy to introduce the plasmid into yeast cells, and the copy number of the plasmid is 100 per cell. Furthermore, it also replicates the E. coli as well as in yeast cells. National Institute of Agrobiological Resources Succeeded in the regeneration of wood cell protoplast into the complete plant.	

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BIOTECHNOLOGY

R & D, STRATEGY OF SEED INDUSTRY DISCUSSED

Tokyo BIO INDUSTRY in Japanese Jan 86 pp 62-68

[Article by Saijuro Kaneko, president of Kaneko Seeds Company]

[Text] In spite of potential technological advancement and breakthroughs, I believe that the main plant propagation process of the future will rely on seeds as in the past, because of their stability, simplicity and storing convenience. As business strategies, nursery companies set up a goal to develop superior hybrid seeds and we are keenly interested in the role of biotechnology in this context. Considering collection of genetic resources and market needs, I suppose that internal and external inter-business affiliations and internationalization of businesses will be more eagerly promoted.

1. History of Seed Industry

Before pondering future business strategies of nursery companies, we must understand the historical background and present facts of Japan's seed industry. Aside from the socialist countries, seed distribution today in various countries can be divided into three types according to the developmental stage of the country. Countries in the first step of development have absolutely no seed production and distribution structures. In these countries seeds are available on a self-sufficient basis. Farmers collect their own seeds necessary for the next year's planting. In countries in the second step of development, commercial seed dealers are engaged in distribution of seeds only on an individual scale as seen in many developing countries in the democratic bloc. Seed dealers do not grow or collect seeds but purchase and sell surplus seeds collected by farmers for their own use. In countries considered to be in the third step like Japan, business entities breed seeds, systematically collect them and then export them overseas. Only the United States, EC countries and Japan are in this step, and a number of countries (Korea, Taiwan, countries in South America and New Zealand are coming closer to this stage).

The Japanese nursery industry has also come through processes similar to the first and second steps. Precisely, in the Tokugawa era, a so-called seed business emerged (first step), and it has gradually evolved into the third step period since the Meiji era. The Meiji government, under the banner of civilization and enlightenment, vigorously imported American and European technology. Many new strains of plants were imported to Japan in this era. On the other hand, many Brassica vegetable seeds were brought to Japan from China through military services in the Sino-Japanese War and Russo-Japanese War. These imported strains were studied for breeding by conscientious farmers and associated seed dealers (seed dealers then were proprietors) and at government and local community laboratories. In 1890, the Yokohama Ueki Company was incorporated for the first time in Japan, and it contributed greatly to the introduction of foreign strains.

From around the beginning of the Showa era, studies on the first generation hybrids (F_1 hybrid) was about to be put into practical use primarily in vegetables. After World War II, private businesses competed in announcing their F_1 hybrids. Now the majority of vegetable seeds in Japan are the F_1 hybrids. The number of major vegetable strains and the percentage of F_1 hybrids are as indicated in Table 1, compiled by the Japan Nursery Association's (corporation) committee for preventing duplication of names of strains.

F_1 strains which make use of this heterosis are homogenous in phenotype according to the Mendel's Laws of Heredity. The F_2 from the F_1 will show various divergent characters. This enables monopolized continued sales of seeds, and opens the door to overseas sales routes, contributing to the expansion of markets and an extremely advantageous situation for the nursery business.

On the other hand, the "Seed Name Registration System" (1948) was enforced from the standpoint of protecting seed breeders and popularizing superior strains. Also, a new "Seed and Seedling Law" was promulgated in 1978, equivalent to a plant patent, from an international perspective. Additionally, in conjuntion with the recent establishment of the so-called biotechnological engineering processes which make it possible to study breeding in units of cells, the seed industry has attracted the spotlight.

2. Characteristics of Japanese Seed Industry

In 1983, the American Seed Association's 100th Anniversary Convention was held in San Francisco. The length of its history is not significantly different from the Japanese nursery industry. However, the contents are considerably different due to the gap in eating habits and in distribution of genetic resources.

Americans and Europeans, mainly meat eaters, bred corns and sorghums necessary for production of cattle, and proceeded with hybrid research.

On the other hand, in Japan where fish and shellfish were staple foods, breeding of rice and wheat was undertaken in the natural order of a rice country. Consequently, the scope of the seed industry was inevitably limited to vegetables and flowers. In vegetable breeding, especially in breeding of Brassica vegetables indigenous to the soil of the East, Japan has grown to be one of the world's leading breeders. The Japanese people are scrupulous and diligent. Japanese Americans, who immigrated to California, first made their success in vegetable and flower growing. Similarly, in Brazil, Japanese descendants were successful in vegetable and flower cultivation. Characteristics of the Japanese people are well suited for such work as breeding which requires patience, scrupulousness and dexterity.

The major crops of Japan, rice, wheat and soybeans, are under government management. These seeds are bred by national and public breeding agencies. Seeds are circulated through an established route from a prefectural government to an agricultural organization and to a farming household based upon the "Main Agricultural Crop Seed Law," which does not leave any room for private business to intervene. Therefore, Japanese nursery operators have engaged mainly in vegetable breeding and adjunct flower breeding. Because of the size of the market, the operational scale was inevitably small. At present, the total vegetable farming area in Japan is 650,000 ha, which is somewhat in excess of 10 percent of the total farming land of 5.4 million ha. The flower growing area is about 25,000 ha. As for stock raising, nearly 100 percent of feed grains are imported, except for the green fodder for cattle that requires 900,000 ha.

In comparison, breeding technology in Japan is far superior to that in other countries. The dissemination rate of hybrid vegetable seeds is several times higher than that in Europe and America. A sizable quantity of Brassica vegetable seeds are exported by Japanese nursery companies to Europe, America and other countries in the world. What is more impressive, virtually all of them are hybrids. Table 2 indicates seed exports/imports of Japan as of last year.

The unit price of exports is 10 times the unit price of imports. In addition, half the imported seeds are produced in foreign countries under a contract using original seeds such as the open-shell shaped radish seeds provided by Japan.

3. Is the Seed Industry Profitable?

In the last 10 to 15 years, we have heard a lot about buying-out and reorganization of European and U.S. seed companies. It is naturally understandable for (Cargill) (major grain company) and Anderson, Clayton and Co. (Food Oil Fat Company) to make such a move. However, chemical companies and petroleum companies have also competed in buying out seed companies. Recently there was a case where a seed company which was bought with much trouble was resold at a price lower than half of the purchase price. Keystone Seed was

previously bought-out by Union Carbide, but it was recently placed under the umbrella of Agrigenetic. MMC sold Niagra Seed to (Celler) Seeds. Lately, (Celler) Seeds sold, in one package, previously purchased Harris, (Moran) and Niagara. Why did they have to sell what they once exerted themselves to buy? One American involved in such a transaction made a remark: "Seed companies have many special aspects that are managed by incomprehensible policies." The truth of the matter is that outsiders cannot understand this business too well. When we visit a bought-out seed company, the owner will not show up. Equipment is improved but the same old faces are there to help us. In the crop breeding field, results will not always coincide with the blueprints which instruct what kind of varieties should be grown in a fixed number of year's plan and how much revenue should be expected from the work. Successful results will bring a large income, but results show up slowly after many years, even when much capital is invested. A failure in developing strains literally means more risks to be shouldered by the company. The new owner might have judged that a further involvement in the seed business is too risky, and probably thought it wise to sell it even at half the purchase price.

Then, why do big businesses cast a passionate eye on the seed industry? I have considered various angles and come up with the following assumptions: 1) Future food shortages are forecast by the United Nations or other organizations, and it is assumed that the breeding of crops will play a significant role in the stable supply of food; 2) Food in every country is standardized. A market for one strain is being expanded. European, American and Chinese strains have access to the Japanese market. Conversely, Japanese strains are marketed in Europe; 3) In major countries in the world, a new strain protection system is established and breeders' patent protection is systematized. With this system, it is pleasantly estimated that the private business' development investment can be recovered; 4) Compared to other industries, this industry will be less affected by the economic slowdown, and a structural slump is unthinkable. Also, it claims a high earning rate; 5) With the progress of breeding technology, hybrids are available for various strains. This enables monopolized continued sales; 6) By new bioengineering techniques, various unknown fields such as mutation, gene recombination and cell fussion, evolved and offer lots of possibilities.

These are the positive factors that I can think of. In essence, however, the seed industry promised a bright future and high earnings but is balanced by risks of unknown factors, long and tedious research time and lack of certainty. It takes too long to get some results for a new participant. Usually new entrants resorted to an easy method of buying-out an existing seed company, and conversely sold it before taking a high risk on the specificity of the business.

Although I have cited various positive factors in the above, it is the hybrid seeds that to date have supported the growth of the nursery companies. Promising future, international potential and high earning efficiency of tomorrow's seed industry will all come true with the development of hybrid seeds. It is not an overstatement to assert that the rise and fall of nursery companies rest upon the development of hybrid seeds.

4. What Are Hybrid Seeds?

In Japan, hybrid is called "crossed variety of the first generation (F_1)." It means the hybrid of the first generation, and only the first generation exhibits a special superior character resulting from pairing specific parents. Second and subsequent generations will lose that special quality. In genetic terminology, the phenomenon which manifests this superior character is called "heterosis." Parents used for this purpose must be selected from perfectly fixed strains (linage without variations). Also, it is proven that the heterosis appears stronger when the lines between the parents are farther apart.

Hybrid seeds are produced using various methods by utilizing the plant's nature of sex differentiation with evolution. In plants, sex differentiates with evolution as shown in Figure 1 from most undifferentiated single cell organisms such as viruses and bacteria. Flowers which have both the stamen and the pistil in one flower are bisexual. Bisexual crops are further divided into a compatible type whose own flower pollen are highly compatible with its own stamens and into a self-incompatible type whose pistils are not fertilized by its own stamens but by pollen from other flowers. With the further advancement of evolution, crops like the melon family emerged, which have male flowers exclusively with stamens and female flowers exclusively with pistils. Plants most advanced in sex differentiation are dioecious, and they come with male plants which only grow male flowers and female plants which only grow female flowers. Among vegetables, spinach and asparagus are dioecious plants. Also among plants, unwholesome male flowers sometimes blossom without pollen. These are called sterile male plants. Research is underway to produce hybrids using the cytoplasmic inheritance of this sterile male plant.

Hybrid seeds obtained from completely fixed parents will satisfy conditions such as superiority (vigor, high yield and disease-proof), perpetuity (manifestation of same character year after year) and homogenuity (uniformal), and will be most ideal as seeds for crops. However, seeds collected from the first generation hybrids (hybrid seeds) will lose economic value in accordance with the laws of heredity. Therefore, hybrid seeds must be bought every year from a nursery company which stocks their parents. If hybrid seeds are developed with special qualities such as a 50-percent higher yield, strong resistance to diseases and very tasty, they can command a high price every year for that added value. These principles of hybrids are utilized not only in plants but also in animals. It is also used for breeding chickens and pigs in America.

Following is the currently considered hybrid seed breeding methods which make use of these plant characteristics.

4.1 Artificial Crossing

This is the most classical hybrid culture method. Plants are castrated by human hands and paternal pollen are pollinated also by human hands. Vegetables and fruits such as tomatoes, eggplants, cucumbers, watermelons and melons are presently crossed by this method. Use of this method is limited to crops that yield plenty of seeds from one crossing operation and can command a high price in relation to grain seed.

4.2 Use of Self-Incompatibility

This hybrid culture method uses a character of a mature flower that does not fertilize its own pistils by its own pollen. In order to make original incompatible seeds, bud pollination is performed. Bud pollination requires artificial crossing. A lot of Brassica genus (chinese cabbage, cabbage, broccoli, cauliflower and the like which blossom cruciform flowers and belong to the Cruciferae) vegetables are the paramount speciality of the Japanese nursery companies because many of them are originated in the East and artificial crossing is used for bud pollination.

4.3 Use of Male Sterile Plants

This is a hybrid culture method which utilizes the cytoplasmic inheritance character of male sterile plants after finding defective flowers which do not produce pollen. This method was researched in the United States using onions at the beginning of the Showa era. Practical varieties were developed in onions and carrots which rather frequently manifested male sterility and were easy for preserving stocks. This method is considered to be in the future mainstream of breeding. Hybrid rice seeds are also collected by this method which utilizes male sterility. I have a feeling that this seed collection method will be considerably adopted when the mass cell culture method is established by biotechnological engineering.

4.4 Use of Unisexual Flowers

This is a method which physically removes male flowers. A famous example of this is the corn hybrids. Using the character that male flowers develop on the top of a plant, hybrid seeds are grown by removing the stamens.

4.5 Use of Dioecism

In spinach, seeding of male plants occurs earlier than that of female plants. In this method, the difference in timing of seeding is utilized and plants of early seeding are pulled out before blossoming. When the clone propagation technology is established in biotechnology, it will become possible to propagate only male plants or female plants in a flask.

4.6 Use of Chemicals

Also, self-pollination can be prevented if anthers or pollen are selectively killed or inhibited from growing by spraying chemicals. Pharmaceutical companies are undertaking research in this field.

The above described methods are currently considered hybrid seed development methods. Whether we can develop hybrids more accurately and simply and how we can use biotechnology in this field are the primary concern of nursery companies.

5. Biotechnology and Seed Industry

Recently, biotechnology in Japan and foreign countries has made remarkable progress in basic technology, and reactions of Japanese nursery companies in this field are awaited. However, Japanese nursery companies are small on the business scale while considerable capital burdens are required in the basic biotechnology research of high development risks for introducing new research facilities and human resources and accumulating relevant technologies. Therefore, the Ministry of Agriculture and Forestry and Fisheries planned the "High Standard Nursery Technology Development Project" to promote joint development with the private sector of the breeding by tissue culture expected from early practicalization and seed preparation technology. The Japan Nursery Association was designated as the main body for the project. The Nursery Association plans to implement the project in 5 years from 1983-1987, and installed a "High Standard Nursery Technology Development Committee" of 12 professional authorities on tissue-culture from test and research organizations of the Ministry of Agriculture and Forestry and Fisheries, universities and the private sector in order to verify the role of nursery companies in biotechnology, evaluate relevance to studies conducted by the government and universities and to manage the project efficiently. In this committee, trends of foreign and domestic research on tissue culture technology were documented and subjects for technology development of the project were selected. The following four groups were organized for each subject and the research project started in FY83. Currently, the project is in the third year.

Subject 1: Promote mass propagation technology for superior seeds and seedlings by tissue and cell culture

Subject 2: Seed collection by shoot apex culture and clone propagation technology for breeding parent specimens

Subject 3: Breeding efficiency improvement technology by anther and pollen reproductive cell and organ culture

Subject 4: Variation inductive and selective technology by callus and cell culture

As for the gene recombination technology and cell fission technology currently recognized to be the special advanced technologies, corporate research should wait until government laboratories and universities acquire some technical understanding and open the way for practical development since there are still a lot of unknown elements in this field. The committee concluded that the immediate research goals should be focused on the mass propagation technology for seedlings free of virus diseases by the practical shoot apex culture and the prompt mass propagation technology for superior seeds and seedlings by the cell and tissue culture expected from comparatively early practicalization. Even with the latter prompt mass propagation technology, a significant incidence of variations occurs in some crops during the culture process at the present stage. Theories and facts seem to be at a considerable distance.

The current business strategies of nursery companies are focused on the establishment of technologies such as propagation of disease free seedlings, clone propagation of male sterile plants and tissue prompt mass propagation. These technologies will lead to the research on hybrid plant culture and growing artificial seeds from embryonic derivatives. This implies that the success in the mass propagation of embryonic derivatives and the resulting resolution of the variation, storage, germination and cost problems, is expected to deliver a technology extremely revolutionary even to the nursery industry.

Also, cells and tissues in culture callus and produce variations. In order to develop new varieties by utilizing the variations, the following tests might be required: positive variations induction tests with gamma rays, tests with mutation inducers, tests for utilization of chimera cells and tests to find cells that genetically retain superior characteristics such as being disease proof, weed-killer resistance and high amino acidity.

6. Future Strategies of Nursery Companies

It is not easy to draw a conclusion about the tactics and strategies of nursery companies at today's high tech dawn when new technologies are rapidly being developed. It is currently expected that biotechnology and hybrid growing technology are expected to make a significant advance. In addition, we are expecting the arrival of other entirely new technological developments.

On the other hand, the Ministry of Agriculture and Forestry and Fisheries opened the door to the private sector of the rice and wheat seed research which was previously set apart as a sacred government field. That indicates a future liberalization of seed distribution. Consequently, with that kind of a promising picture, big businesses are expected to make research investments concentrating on this area. Nevertheless, I believe with certainty that the propagation of plants today and tomorrow will evolve around the propagation of seeds considering various conditions such as simplicity, storing convenience and variations. It, therefore, amounts to how we can develop superior seeds into hybrids. Henceforth, we will be anxiously observing how new biotechnology can be applied to fulfill this purpose.

Also, no matter how biotechnology advances, we still have a major problem of preclusive genetic resources. It takes lots of capital and many years to gather genetic resources. In this view, existing nursery companies have a big edge as they maintain a rather large collection of phyletic lines of vegetable and flowering plants. Also, as a task after the completion of the biotechnological work, it will become necessary to investigate actual cultivation in gardens. There will be many cases where several years of research by conventional breeding procedures are needed for the development of practical new strains. Furthermore, even when a new strain is developed, it will require a decent organization of its dissemination and marketing. If businesses other than nursery companies take an interest in getting involved in the plant biotechnology, they will probably need to have some form of contact with nursery companies. It is no wonder that European and American big businesses buy out nursery companies.

The nursery companies of tomorrow may be able to expect large capital investments, escalated internationalization of crop strains and market expansion, pointing to a progressive internationalization in technology, seed collection and marketing.

Table 1. Percentage of F_1 in Major Vegetable Strains

種類名 (1)	品種数 (2)(A)	うちF_1 (3)(B)	F_1の割合 (B/A)(4)
(5) キャベツ	372	351	94.4
(6) はくさい	309	280	90.6
(7) ほうれんそう	162	97	59.5
(8) レタス	88	0	0
(9) カリフラワー	83	50	60.2
(10) ブロッコリー	44	40	90.9
(11) メキャベツ	8	6	75.0
(12) ねぎ	70	3	4.3
(13) たまねぎ	90	36	40.0
(14) きゅうり	444	357	80.4
(15) トマト	271	206	76.0
(16) なす	168	141	83.9
(17) かぼちゃ	88	60	68.2
(18) ピーマン・とうがらし	94	40	42.6
(19) だいこん	268	98	36.6
(20) にんじん	193	22	11.4
(21) すいか	262	228	87.0
(22) メロン・まくわ	232	157	67.7
(23) その他22野菜	655	81	12.4
(24) (計) 44 野菜	3,901	2,253	57.8

[Key on following page]

Key:

1.	Name	13.	Onion
2.	Number of strains	14.	Cucumber
3.	Number of F_1	15.	Tomato
4.	Percentage of F_1	16.	Eggplant
5.	Cabbage	17.	Pumpkin
6.	Chinese cabbage	18.	Green pepper and red pepper
7.	Spinach	19.	Radish
8.	Lettuce	20.	Carrot
9.	Cauliflower	21.	Watermelon
10.	Broccoli	22.	Melon and musk melon
11.	Brussel sprouts	23.	Other 22 vegetables
12.	Stone-leak	24.	(Total) 44 vegetables

Note: 1. From "Vegetable Variety Book" by Japan Nursery Association (Co.) (1982.3)

2. It is assessed that there are about 3,000 varieties other than these listed in the table primarily among local (native) varieties.

Table 2. Export/Import of Seeds and Seedlings
(Monthly Trade Bulletin Plant Quarantine Data) (unit/million yen)

(1) 輸出

	S54	S55	S56	S57	S58	S59
(2) 野菜種子 (t)	345	390	437	435	584	472
(3) (額)	2,486	2,512	3,010	3,791	4,653	4,214
(4) 花種子 (t)	6	7	6	7	8	9
(5) (額)	472	557	766	1,120	1,226	1,693
(6) 計 (t)	351	397	443	442	592	562
(7) (額)	2,958	3,069	3,776	4,911	5,879	5,907

(8) 輸入

	S54	S55	S56	S57	S58	S59
(9) 野菜種子 (t)	2,604	3,079	3,301	4,850	8,758	8,793
(10) (額)	1,921	2,307	2,321	4,244	6,414	6,187
(11) 飼料種子 (t)	12,387	13,332	13,224	12,481	12,728	12,789
(12) (額)	3,088	3,592	3,648	3,770	3,728	3,733
(13) 計 (t)	14,991	16,411	16,525	17,331	21,486	21,582
(14) (額)	5,008	5,899	5,969	8,014	10,142	9,920

(15) 輸出入種のkg当り単価 (16) (円単位)

	S54	S55	S56	S57	S58	S59
(17) kg当り価格 輸入	737	749	703	875	732	703
(18) 輸出	7,205	6,441	6,887	8,714	7,967	8.927

[Key on following page]

Key:

1. Exports
2. Vegetable seeds
3. Sum
4. Flower seeds
5. Sum
6. Total
7. Sum
8. Imports
9. Vegetable seeds
10. Sum
11. Feed seeds
12. Sum
13. Total
14. Sum
15. Export/import seeds price/kg
16. Unit: yen
17. Import price/kg
18. Export price/kg

Data has significantly changed since FY82 tracable to the over-importation of vegetable seeds (mainly open-shell shaped radishes)

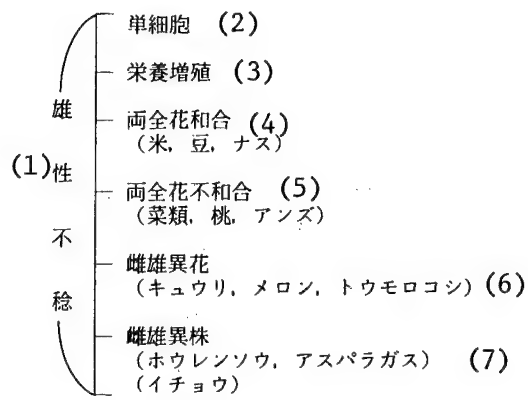

Figure 1. Sex Differentiation Process

Key:

1. Male sterility
2. Single cell
3. Vegetative propagation
4. Bisexual (rice, beans, eggplants) compatibility
5. Bisexual (greens, peaches, plums) incompatibility
6. Unisexual flowers (cucumbers, melons, corns)
7. Dioecism (spinach, asparagus) (ginko)

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NEW MATERIALS

TRENDS IN INFRARED OPTICAL FIBERS DISCUSSED

Tokyo CERAMICS JAPAN in Japanese Jul 85 pp 595-600

[Article by Shiro Takahashi, Ibaraki Electrical Communication Laboratories, Nippon Telegraph and Telephone Corporation: "Optical Fibers for Infrared Rays"]

[Text] 1. Introduction

Recent years have seen remarkable progress in research and development of machines and equipment for information transmission on which are based the evolution of a sophisticated information society. Above all, research in what is called the optoelectronic sector, the sector of machines and equipment for optical transmission of information, is going forward in an aggressive manner. Optical fiber is the medium for the optical transmission of information and is playing an important role in the industry of optical transmission of information. Optical fiber is a type of ceramics.

Major features of the fiber are: high transmission of light (flexibility); reduced attenuation (low transmission loss); ability to transmit large quantities of information (large capacity); lack of susceptibility to electrical noise (non-inductive); lightweight and is fine in diameter (small in weight and in diameter). Because of these properties, optical fiber is finding a wide range of applications, from transmission mediums for optical communications, which are of lengths measured in kilometers, to light guides of lengths measured in meters. It is particularly notable, at this juncture, that, contrary to optical fibers of the silica type, which have already been commercialized, infrared optical fibers that permit transmission of light of wavelengths in the range of 2 to 10- μm--intermediate infrared rays--are seeing exploration of new applications on the basis of its feature of infrared ray transmission.

2. Optical Fiber Structures and Features of Light Transmission Loss

The structure of optical fiber for light transmission is basically composed of a section that permits light transmission, referred to as the core, and a section that is of lower refractory indices, referred to as the clad. Those devices which have long been known as light guides, etc., involve large differences between the refractory indices of the core and the clad and permit

transmission of large quantities of light energy. Nevertheless, a device with such a structure permits dispersion of light to a large extent and has only a limited capacity for transmission.

Thus, it is not adapted to optical communication of transmission of information by means of pulse signals. As seen in Figure 1, such wave transmitting structures are designed for optical communication purposes: a) a structure referred to as the step type, where the difference in both the index and the dispersion are reduced; b) a structure referred to as the graded type, wherein the refractory indices in the core vary gradually, so that its capacity for transmission is increased; c) a structure referred to as the single mode type. It has the largest capacity for transmission of all types. An optical fiber grows more valuable as the attenuation of light that it transmits decreases, whether it is used for transfer of energy or transmission of information. The light transmission loss is made up of absorption loss and scatter loss, and each loss is partly due to the unique properties of the material and partly caused by impurities and defects. Figure 2 shows these loss factors diagrammatically.

The ultraviolet absorption edge and infrared absorption edge are due to losses inherent in the raw material. Absorption losses not inherent in the material include electronic absorption caused by impure elements such as transition metals and rare earth elements and the molecular absorption caused by such impurities as the hydroxyl group. Absorption produced by defects in the material, such as the dangling bond--referred to as WAT or weak absorption tail--is also conceivable. These may be inherent factors if the quantity of defects is determined by thermal equilibrium conditions exclusively. In many cases, nevertheless, they are affected by manufacturing conditions.

Scattering loss, α_s, of optical fiber is given by the formula

$$\alpha_s = \frac{A}{\lambda^4} + \frac{B}{\lambda^2} + C$$

where λ denotes the wavelength, A a coefficient for the Rayleigh scattering, and B and C coefficients for defect scattering. The Rayleigh scattering represents a loss inherent to the material, and arises from the fine variation in refractory index occuring in the material. The coefficient A varies with the refractory index and the fictive or assumed temperatures of the glass. Defect scattering, on the other hand, is produced by bubbles, fine crystals or undulating core-clad interfaces, among other reasons. This scattering represents a loss from manufacturing conditions and hence, is, removable.

On the assumption that all removable factors have indeed been removed, one can estimate the minimal loss value as the sum of the loss factors inherent to the material: That is, a sum of absorption in the ultraviolet region (Urbach tail), absorption in the infrared region (multiple sound absorption), and the Rayleigh scattering. The wider the material's range of wavelengths permitting light transmission, the lower the material's transmission loss will be. The minimal loss of silica type glass is estimated at 0.2 dB per km (at wavelength

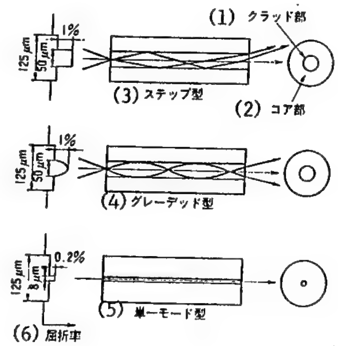

Figure 1. Wave Transmitting Structure of Optical Fibers

Key:

1. Clad part
2. Core part
3. Step type
4. Graded type
5. Single mode type
6. Refractory index

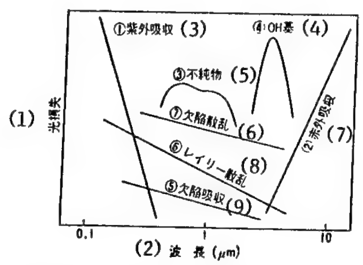

Figure 2. Diagram for Various Factors in the Transmission Loss of Optical Fibers

Key:

1. Optical transmission loss
2. Wave length
3. Ultra-violet absorption
4. OH group
5. Impurities
6. Scattering due to defects
7. Infrared absorption
8. Rayleigh scattering
9. Absorption due to defects

1.55-μm) and that of fluoride glass is estimated to be of the order of magnitude of 10^{-3} per km (at wavelength 3-4-μm).

3. Research Trends for Infrared Optical Fibers

3.1 Materials for Infrared Optical Fibers

Materials adapted to infrared optical fibers, which are characterized by the transmission of infrared rays, may be largely classified into two types, glass and crystals. Table 1 presents various materials and their range of wavelengths for light transmission. The transmission range for bulk glass of the silica type is 0.12 to 4.5 μm, extending from ultraviolet to infrared rays. Fiber of the same type, however, does not permit passage of light in the intermediate infrared range of wavelenghts of over 2.4 μm (where the loss exceeds 1 dB per km). Glass of the fluoride type has transmission ranges from 0.25 to 10 μm, extending deep into the intermediate infrared region. It is, therefore, a highly prospective material for infrared optical fiber. Glass of the chalcogenide type with a transmission range from 0.6 to 15μm has its transmission spectra terminated in the visible region at one end. Therefore, it exhibits coloring or metalic sheen. This type of glass yet displays a wide "window," up to 10 μm or more, for the passage of infrared rays and meets the requirements for infrared optical fiber. KRS-5 and other crystalline materials represent conventional material for transmission of infrared rays. They have, thus far, been applied in general optical systems. These halide crystals also have wide "windows" for transmission and have been studied as materials for optical fiber. The crystals, however, pose more technological difficulties in the preparation of long fiber than do glass materials.

One objective of studying materials for infrared optical fiber concerns utilization of their characteristics of passing infrared rays. One example is transfer of high energy by means of a 1.06 μm-YAG [yttrium-aluminum garnet] laser and a 10.6 m carbon dioxide gas laser. Another is sensoring of temperature by transmitting thermal radiation rays. The other related objective is to explore the possibility of producing optical fibers of ultra-low transmission loss which supersede the performance of current optical fiber for communication of the silica type.

Research on optical fibers began in the 1960's and gathered momentum following attainment of a level of transmission loss of 20 dB per km in 1970. Figure 3 shows the process of lowering transmission loss for optical fiber. Reduction of transmission loss using glass of the silica type as materials advanced, and in 1979 attained a value of 0.2 dB per km, which must be the ultimate for the material. Research on infrared optical fibers since then has quickened with the use of other materials. Described below is the trend of research on optical fibers using fluoride glass, chalcogenide glass, and halide crystals as materials.

3.2 Optical Fluoride Fiber

Typical compositions of fluoride glass, for which research is now underway in connection with optical fibers, are presented in Table 2. Glass in which the major constituent is ZrF_4 has a comparatively short history, its first

Table 1. Materials for the Transmission of Infrared Rays and Wavelength Ranges

Material	Composition	Transmission Range (μm)
Glass		
Quartz	SiO_2-GeO_2, F	0.12 - 4.5
Fluoride	ZrF_4-BaF_2-GdF_3-AlF_3	0.25 - 10
Chalcogenide	As-S	0.6 - 13
	As-Ge-Se	0.8 - 19
Crystal		
Single crystal	CsBr	0.3 - 55
Polycrystal	KRS-5 (TlBr-TlI)	0.6 - 40

Table 2. Composition of Fluoride Glass for Optical Fibers

Glass	Composition (mol percent)									
	ZrF_4	BaF_2	LaF_3	GdF_3	YF_3	AlF_3	PbF_2	CaF_2	LiF	NaF
1	61.8	32.3		3.9		2				
2	57.5	33.5	5.5			3.5				
3	57	36	3			4				
4	60	31	1	4		2.5	1.5			
5	51	16	5			3	5		20	
6	58	15	6			4				21
7		20			17	43		20		

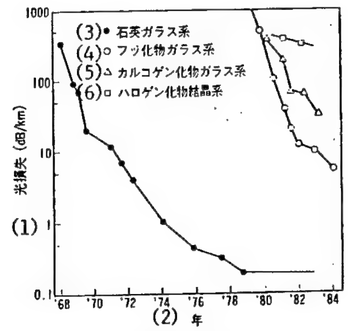

Figure 3. Annual Declines in the Value of Transmission Loss for Optical Fibers

Key:
1. Optical transmission loss
2. Year
3. Silica glass type
4. Glass of the fluoride type
5. Glass of the chalcogenide type
6. Crystals of the halide type

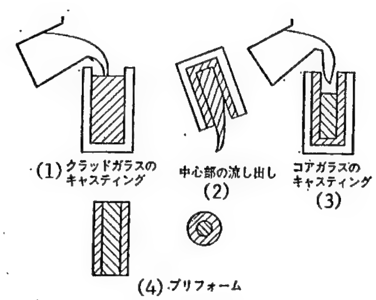

Figure 4. Method of Manufacture for the Preform of Fluoride Optical Fibers by Means of Built-In Casting

Key:
1. Casting of clad glass
2. Central cylindrical portion is poured out
3. Casting of core glass
4. Preform

appearance was in France in 1975. Nevertheless, this glass has drawn attention as infrared optical glass because of the wide range of wavelengths in which light is transmitted, and for the stability it exhibits. Glass of the composition given in Table 2 is more stable against crystallization than are other fluorides, but also more subject to crystallization than ordinary glass of the oxide type. Fluoride glass, therefore, requires rapid quenching for its manufacture and is actually subjected to manufacturing methods entirely different from those for silica glass, where production of optical fiber is concerned.

In fusing fluoride glass, one must exercise care to avoid mixing oxygen and water of the atmosphere just as one must remove impurities like transition metals. OH-impurities, with a major absorption peak at 2.9 μm of wavelength, affect absorption loss of fluoride optical fibers to a large extent. Oxide impurities form cores of crystallization in the fluoride melt, thereby rendering inherently unstable fluoride glass more susceptible to crystallization. Purified materials of the glass, therefore, are subjected to a comprehensive fluorination treatment by NH_4HF_2 etc. and subsequently melted are turned into glass under a dry and inert atmosphere.

The production of optical fiber, meanwhile, is based on the preform method and various methods unique to fluoride glass were devised to prepare preforms of wave-transmitting structure. For example, a "built-in casting method" and a "rotational casting method" were created. In the built-in casting method, a melt of clad glass is cast into a mold made of brass and a central section of the cast. Before that portion has solidified, it is poured out as in Figure 4. The resulting cylindrical hollow portion is filled with a core-glass melt such that a wave transmitting structure of the step type is produced. One characteristic of this method is the casting of the melt, which is adapted to the requirement of rapid quenching for fluoride glass. Another is the formation of core clad interface by the smooth liquid surface involved. Processing of preforms into optical fiber, i.e., drawing them into lines, requires that the preform be softened at temperatures below its crystallization. The method adopted is to draw the preform into lines jacketed with a tube of fluorine resin, having the same softening temperature as the preform. If the preform is drawn naked in the air, crystallization often occurrs at the surface.

Figure 5 presents a transmission loss spectrum of an optical glass fiber of the series ZrF_4-BaF_2-GdF_3-AlF in which a minimal value of 6.3 dB per km has been attained for transmission loss.

The steep rise of the curve from wavelength 3.5 μm upward corresponds to the infrared multisound absorption edge. The peak at 2.9 μm is due to the hydroxyl group and the one at 1-2 μm due to ions of impure metals present in very small quantities. The quantity of impure elements in this fiber is estimated to be below 1 ppm. The loss due to scattering is substantial, amounting to 20 dB per km at wavelength 1 μm. The scattering may conceivably be due largely to defects of the glass.

Fluoride optical fibers of the single mode type are also being produced. With a cutoff frequency of 2.7 μm, and a difference in refractory index of

0.3 percent, this type can have a core diameter as large as 18 μ m. The long wavelengths used serve to reduce connection losses. Fluoride glass has smaller raw material dispersion than silica glass with a zero-dispersion wavelength of around 1.6 μ m.

3.3 Optical Fibers of Chalcogenides

Chalcogenide glass for optical fiber has been investigated in connection with As-S series, As-Ge-Se series, and Ge-S series, etc. The As-S series of glass is the more stable of the two components and displays a red color with a transmission window of 0.6 to 13 μ m. The As-Ge-Se series does not transmit light in the visible region and shows a metalic sheen with a transmission window of 0.8 to 19 μ m. It may find application as a medium for the transmission of CO_2-gas lasers of wavelength 10.6 μ m, though a glass series containing Te is favored for the material. The Ge-S series, free of arsenic, features non-toxicity and exhibits a yellow color with a transmission range of 0.5 to 11 μ m.

Preparation of chalcogenide glass is carried out in a sealed quartz ampule because of the high vapor pressures of the component elements and because of the high susceptibility of the elements to oxidation. The stability of the glass against crystallization is greater than for fluoride glass and permits preparation of optical fibers by use of the double pot method.

The feature of transmission loss for optical fibers of chalcogenides is that absorption peaks in the range of 2 to 5 μ m due to SH and SeH. Also OH impurities are an obstacle in attaining a low loss and that absorption due to defects of the material itself, such as dangling bonds, (weak absorption tail) is large. Figure 6 gives a spectrum, plotted against photon energy, of the transmission loss of optical fiber of the As-S series, where a minimum of 35 dB per km at wavelength 2.44 μ m, the lowest of all chalcogenide optical fibers, was obtained. The short wavelength side represents the visible region of the spectrum as measured on the bulk glass. That portion of straight line in the range of 1 to 2 μ m corresponds to the weak absorption talk. Assuming that the line represents transmission losses inherent to the material, the estimated minimal loss for this series of glass must be around 10 dB per km. At around 5 μ m, a loss of below 200 dB per km materializes. This value is the lowest of all optical fibers and is the most favorable in connection with the power transmission of carbon monoxide laser of wavelength 5.3 μ m.

3.4 Optical Fiber of Crystals

The optical fiber first studied for the transmission of infrared rays was fiber of polycrystals involving KRS-5. Polycrystal optical fiber, as currently produced by the extrusion method, may involve AgCl-AgBr as the raw material, or KRS-5, i.e., TlBr-TlI or other materials. None of these, however, is amenable to drawing for long-distance application. As seen in analyses of transmission loss due to scattering, in preparation of single crystal fiber involving CsI, etc., research on low transmission loss of crystal optical fibers is moving ahead aggressively. Nevertheless, a value of the loss below 50 dB per km has yet to be attained. These fibers, in spite of the above failure, represent the only medium for transmitting CO_2 laser power

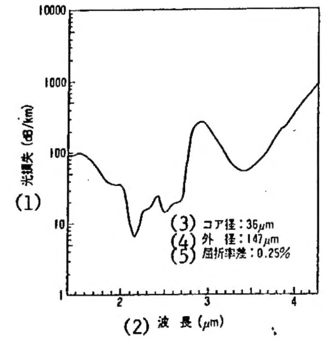

Figure 5. Spectrum for Transmission Loss of an Optical Fiber of the ZrF_4-BaF_2-GaF_3-AlF_3 Series

Key:

1. Optical Transmission Loss
2. Wavelength
3. Core diameter
4. External diameter
5. Difference in refractory index

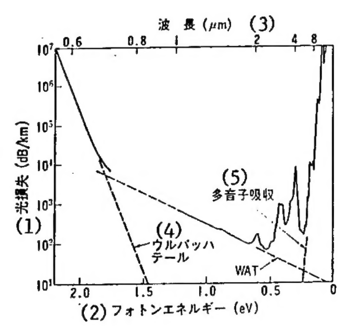

Figure 6. Spectrum for Transmission Loss of an Optical Fiber of the As-S Series

Key:

1. Optical transmission loss
2. Photon energy
3. Wavelength
4. Urbach tail
5. Multiple sound absorption

for distances measured in meters and, hence, research is being supported for lower transmission loss and greater stability.

4. Features and Applications of Infrared Optical Fibers

The basic feature of the infrared optical fiber is its favorable transmission of infrared rays. Because its transmission window extends up to 10 μm, one can push ahead with the materialization of an optical fiber of ultra-low transmission loss, so as to apply the result in optical communication, on the one hand, and with the direct application of transmitted infrared rays themselves on the other.

The development of optical fibers of low transmission loss for communication purposes was triggered by the materialization of a fiber which might permit transmission of a capacity equivalent to, or even greater than, that of the coaxial cable. This had a transmission loss of 20 dB per km, a lower value than for the cable. Developmental efforts have finally led to improvement of performance by two digits to 0.2 dB per km. It is conceivable that, in research of optical fibers of ultra-low transmission loss as an application field of infrared optical fiber, materialization of a fiber with a transmission loss equivalent to that for silica type optical fiber may trigger new development, as in the case of silica type fibers. Applications for which the transmission characteristics for intermediate infrared rays of the materials above are directly available are power transmission, infrared image transmission, and sensors. A number of laser beams of high output are found in the infrared region and, though their power transmission is currently carried out commercially by the multiple joint mirror method, the emergence of infrared fibers is making the operations simpler.

Another new field of application of the fiber is being explored in precision machining and in medical instruments, e.g. laser scalpels. Optical fibers of the silica type are satisfactory for YAG [yttrium-aluminum garnet] lasers of wavelength 1.06 μm. However, chalcogenide optical fiber of the As-S series is more adapted to CO laser of 5.3 μm and crystal optical fibers of the AgCl series to CO_2 laser of 10.6 μm. Other applications are: an infrared image quide, wherein infrared optical fibers made into a bundle serve to transmit infrared pictures; a remote-sensor system for temperature which transmits thermal radiation; and a gas sensor which detects the C-H absorption peak in the region of wavelength 3 μm.

5. Conclusion

After much research and development over the past 10 years in optical fibers, the ultimate theoretical limit was attained for the use of glass of the silica type through progress in the science of materials, and in technology for the manufacture of the fiber. Since the manufacture of optical fibers of the silica type has entered the commercial stage with established technologies, research on infrared optical fibers, subsequently, is aggressively advancing.

Though research is still in the initial stage and many obstacles remain, steady progress is being made in connection with technologies for manufacture

and assessment. One may reasonably hope for future development of the fiber aimed at materialization of infrared application technologies and optical fibers of ultra-low transmission loss.

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